# Southern Academic Review


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# Southern Academic Review

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# *Note*

Each paper in this journal serves as an example of the scholarship being produced by students at Birmingham-Southern College. As such, it attempts to reproduce each paper in the format of the discipline in which it was created. Consequently, there are minor inconsistencies of style throughout the publication. These have been retained as a subtle celebration of the diversity that makes *Southern Academic Review* representative of the liberal arts education found at Birmingham-Southern College.

# Euthanasia: An Ethical and Pragmatic Public Policy Approach

Eddie LaCour

The debate regarding euthanasia contains several complex ethical and public policy issues that challenge our most fundamental beliefs regarding life and liberty. Can killing ever be merciful or justified? Do individuals have a right to end their own lives? By what principles can the U.S. government justify its current position on euthanasia? In crafting an ethical public policy regarding euthanasia and physician-assisted suicide, one must consider such issues as the sanctity of life, the value of individual autonomy, and the possible consequences of enacting a policy. Only after considering these points and others can one begin to approach a valuable conclusion concerning such a controversial topic.

Dr. Michael Manning writes, "The basic arguments for and against euthanasia and physician-assisted suicide have remained surprisingly unchanged for centuries" (ix). Similarly, physician-ethicist Ezekiel Emanuel claims, "Articles written on the topic in 1894 could be dated 1994" (qtd. in Manning 15). While many of the issues central to the debate have remained the same, others have undoubtedly been refocused by unprecedented advances in medicine. In 1900, two-thirds of all deaths occurred before the age of fifty-five, and the average life expectancy was forty-seven years. In contrast, by 1990, fully eighty-five percent of all deaths occurred after the age of fifty-five. Additionally, by 1997, the average life expectancy had risen to seventy-six (Scherer, 30). Diseases that, in the past, would have taken lives in days or weeks can now be staved off for months or years.

Countless patients have benefited from these remarkable advancements; however, many in the public fear that this technology can sometimes serve to merely prolong suffering by keeping patients alive when they are so near to death. The New York State Task Force on Life and the Law (NYSTFLL) reports that the widespread success of the book *Final Exit*, a how-to on committing suicide, serves as proof that a substantial number of people have grown

concerned about the dying process (5). Furthermore, in recent years, public opinion has begun to show more support for euthanasia. In 1947, only thirty-seven percent of a Gallup Poll favored physician-assisted suicide compared to sixty-six percent in 1986 and seventy-six percent in 1995. Harris Surveys showed a similar trend from thirty-seven percent in 1973 to seventy-three percent in 1993 (qtd. in Horsfall *et. al* 620).

Within the euthanasia discussion there are several practices which must be properly defined and differentiated. In the current debate, euthanasia is an action taken by another person, typically a physician, to end an individual's life. Voluntary euthanasia is practiced with the consent, either immediate or previously recorded, of the patient. Involuntary euthanasia is a more controversial practice that occurs when a physician terminates the life of a patient without the patient's direct consent. Physician-assisted suicide (PAS) differs from euthanasia in that the physician merely supplies the patient with the means by which life is ended. The patient is still the final causal agent. Lastly, there is the practice of refusal or withdrawal of treatment. In this case, a patient's life-sustaining treatment is refused or ceased with the knowledge that this decision will likely quicken the death of the patient. How one views the differences in these practices greatly influences one's final decision on the acceptability of euthanasia or physician-assisted suicide.

The current position of the U.S. government allows for withdrawal of treatment, as the United States Supreme Court concluded that the right to refuse treatment is a protected "liberty interest" under the due process clause of the United States Constitution (qtd. in NYSTFLL 50). In 1997, this same court upheld bans on PAS in New York and Washington, holding that the Constitution does not provide for a right to die (qtd. in Scherer 12). Many euthanasia proponents argue that there is no significant moral difference between euthanasia, PAS, or withdrawal of treatment; however, the law in all states draws a clear distinction among the acts. In New York, assisting a suicide, except in certain limited circumstances, is a form of second-degree manslaughter. However, euthanasia qualifies as second-degree murder, as the defendant intentionally causes the death of the victim through his

or her direct actions (NYSTFLL 63). Both euthanasia and PAS are currently illegal in every state except for Oregon, which allows only PAS. The position of the American Medical Association (AMA) is similar to that of the U.S. government. In 1973, the organization issued a policy statement declaring:

> The intentional termination of the life of one human being by another – mercy killing – is contrary to that for which the medical profession stands and is contrary to the policy of the American Medical Association.
>
> The cessation of the employment of extraordinary means to prolong the life of the body when there is irrefutable evidence that biological death is imminent is the decision of the patient and/ or his immediate family. (qtd. in Rachels 63)

While the U.S. government and the AMA make the distinction between euthanasia/PAS and withdrawal of treatment, critics assert that such a distinction is not warranted. Many ethicists see no crucial difference in the acts; therefore, supporters of euthanasia argue that the correct label for withdrawal of treatment is passive euthanasia. Gerald Dworkin argues that because most people agree that it is permissible for a patient to deny treatment even when it will result in death (passive euthanasia), a patient should be able to ask for active euthanasia (4). "Turning off or unplugging machines, withdrawing tubes, and the like, are all actions the doctor performs, and over the decision to perform them or not the doctor retains control responsibility" (Frey 24).

James Rachels expands on this thought by attacking the notion that killing is always worse than letting someone die. He brings up two hypothetical cases and asks which one is morally worse. In the first, a man murders his wife because he wants to be rid of her. In the second case, an emergency-room physician sees a patient who is suffering from appendicitis. He could operate and save the patient's life, but he recognizes the patient as a woman against whom he holds a grudge. He purposely delays the operation

until the patient dies. Even though the physician is "letting nature take its course," we are as horrified with the second case as we are with the first. From this point, Rachels suggests that our reactions are not based on the inherent immorality of killing or letting die. They are based instead on the circumstances and motives surrounding the cases (Rachels *Ethics* 76).

Rachels expounds on this line of thought, advancing an argument that attempts to prove that killing is not inherently worse than letting die. First, he appeals to the fundamental logic regarding moral judgments, namely "that whether an action, or a type of action, is right or wrong depends on the reasons that can be given for or against it" (Rachels *Ethics* 76-77). If good reasons can be offered against an action then it is wrong. Most people agree that killing can be justified in certain instances such as self-defense. Why then is it wrong to kill in other circumstances? One reason murder is wrong is because the victim's death brings pain to his family and friends emotionally and perhaps economically. More importantly, the murder deprives the victim of a great deal of life that he would have been able to experience. By this logic, letting someone die need not always be considered wrong. If a terminal patient is near death and further treatment is futile, it is not unethical to cease treatment. However, if you have the opportunity to save a drowning child in a bathtub, it is obviously wrong to do nothing. Your ability to act morally implicates you. If you let her die, her friends and family will suffer, and she will lose the remainder of her life. Rachels thus sums up his argument:

1. For any two actions (or types of actions), if there are exactly the same reasons for and against one as there are for and against the other, then they are equally good or equally bad. One is neither better nor worse than the other.
2. There are the same reasons for and against killing as there are for and against letting die.
3. Therefore, killing is neither better nor worse than letting die.

Therefore, in tragic instances in which the judgment is made that there is no point in prolonging the patient's life, "active euthanasia may be preferable to passive euthanasia" (Rachels *Ethics* 76-79).

Opponents of euthanasia and PAS argue that there are indeed significant differences between these practices and withdrawal or denial of treatment. Dworkin notes that denying an individual the right to withdraw from medical treatment, such as a respirator, is to claim the right to forcibly impose an unwanted invasion of the body upon a competent individual. "It is to commit battery." However, this same ethic does not call for euthanasia or PAS, as denying a patient these measures merely leaves them alone. Dworkin concedes this as a significant ethical difference; but he somehow still claims that it "seems arbitrary for the society to allow one but forbid the other" (68-69).

Despite the arguments of Rachels and Dworkin, many opponents still argue that the final causal agent is an important ethical difference among the three end-of-life options. Euthanasia depends on the physician to act as the final cause of death, typically through a lethal injection. In PAS, the physician does provide a patient the means with which to commit suicide – usually in the form of a prescription pill. However, the patient must still carry out the final act that ends his or her life. The physician may assume that the suicide will likely occur, but it is not certain. Lastly, when treatment is withdrawn from a patient, it is true that the physician often knows that the cessation of treatment will quicken the death of the patient. However, opponents of euthanasia do deem it morally significant that the disease, and not a medicine from the doctor, is the eventual cause of death.

Additionally, Christian religious teachings have long opposed suicide and more recently euthanasia and PAS. In the late Fourth Century, St. Augustine wrote that "Thou shalt not kill" applied in cases of suicide. Moreover, as a human is created by God, that life belongs to God, and only God can choose when that life should meet its end. Aquinas echoed Augustine's views by referencing Aristotle's appeals to natural law as well as noting the commandment "Thou shalt not kill." And while Aristotle allowed for euthanasia in cases of "useless" life, Aquinas maintained the

sanctity of all life, regardless of its quality. He held that suicide violated the meaning of the human person and the nature of human community (Manning 16-17). More recently John Paul II has maintained this view, declaring in 1995:

> I confirm that euthanasia is a grave violation of the law of God, since it is the deliberate and morally unacceptable killing of a human person. This doctrine is based upon the natural law and upon the written word of God, is transmitted by the church's tradition, and taught by the ordinary and universal magisterium. (qtd. in Manning 22)

Similar to the current governmental and medical stances, Catholic doctrine allows the decision to forgo "aggressive medical treatments" (Manning 24). There is a distinction between ordinary/ obligatory treatments required of Catholics and conditions that may make treatment "extraordinary" and no longer required. Five criteria used by Catholic moralists to identify extraordinary treatments include impossibility, excessive effort, pain, expense, and intense fear and repugnance. Therefore, "despite the sanctity of human life, extraordinary means to preserve it are not mandatory" (Manning 19-20).

Proponents of euthanasia often highlight the values of autonomy and individual liberty when discussing the ethics of the issue. R.G. Frey asserts, "Control over our own lives is one of the most important goods we enjoy" (Frey 17). Similarly, John Stuart Mill states:

> The sole end for which mankind are warranted, individually or collectively, in interfering with the liberty of action of any of their number, is self-protection. The only purpose for which power can be rightfully exercised over any member of a civilized community, against his will, is to prevent harm to others. His own good, physical or moral, is not a sufficient warrant...Over himself, over his own

> body and mind, the individual is sovereign. (qtd. in Rachels *Elements* 96)

If euthanasia or PAS were legalized, most proponents argue that it would be available only to those patients who were terminally ill, competent, informed, and who had been treated for depression. If these conditions were met, and the patient voluntarily requested aid in ending his or her life, it would seem that the patient's autonomy would be compromised if the government continued a ban on euthanasia and PAS. In *Can Ethics Provide Answers?*, Rachels argues that, "Euthanasia would, to be sure, shorten the patient's biographical life. But it would not make that life worse. Indeed, it is the patient's own judgment that it would make life better." To further his point, Rachels asks the rhetorical question of which life we would choose: one of eighty-five years and a peaceful death or one of eighty-five years and two months, with the last two months filled with terrible suffering (75). Euthanasia proponents believe that to respect autonomy, every individual should be allowed to make that decision personally if that time ever comes.

Some opponents of euthanasia acknowledge that restrictions on suicide do limit individual autonomy. However, "the bare fact that individual options are constrained does not render such limits unconstitutional. Individuals may not irrevocably waive their right against involuntary servitude, for example, regardless of whether the waiver is knowingly and intelligently made" (NYSTFLL 71). And still others question whether ending someone's life ever respects his or her autonomy. Such a power over human life is seen as equivalent to slavery, intrinsically contradicting the value of autonomy (NYSTFLL 88-89).

"Mercy killing" is a term often given to euthanasia and PAS that denotes the other pillar of euthanasia proponents. Beside autonomy stands mercy, which many advocates see as a justification for euthanasia. If a patient is in unbearable pain that is not likely to get better, and the patient no longer desires to live, it would seem unmerciful to keep him alive any longer.

Again, opponents question whether killing can ever be merciful. Others argue that euthanasia is only merciful after an

exhaustion of all other options, and that this condition is rarely met. In 2001, one of the key findings of the NYSTFLL was that depression and pain are tragically under-treated across the U.S. One study of cancer patients at a major hospital found that nine percent of psychiatric consultations concerned acutely suicidal patients. Nearly all of these patients had a previously undiagnosed psychiatric disorder. After treatment for depression, ninety percent of these patients no longer had suicidal ideation (26). Likewise, other studies have estimated that for ninety percent of cancer patients, pharmacological treatments alone can alleviate pain and symptoms to an extent that patients find adequate (40). Opponents of euthanasia argue that such palliative, end-of-life care is far more merciful and moral than any decision to end a patient's life.

To shape an ethical public policy, one must consider the above arguments carefully, as well as pragmatically reflect on the possible outcomes of a policy. The slippery slope claims of euthanasia opponents have proven to be persuasive arguments against the advancement of euthanasia. These purport that legalization of euthanasia or PAS will lead us down a dangerous ethical path. They assert that life will be devalued, restrictions on the practices will go unobserved, and involuntary euthanasia will be a much more likely occurrence. However, Frey states that slippery slope arguments have been used with such frequency lately that they can almost serve proponents of euthanasia.

> So often has it been predicted that the heavens will fall, that we shall descend the terrible slope of taking life until we reach Nazi camps...that the very fact that the heavens have not fallen and the camps have not reappeared can seem to weaken slippery slope arguments. (43)

Despite this, opponents of euthanasia maintain that the theoretical arguments they advance are compelling and are additionally bolstered by recent studies of the practice in the Netherlands.

The Netherlands has some of the highest health and medical standards in the world, with one of the longest predicted life spans

and more than ninety-nine percent of its citizens covered by health insurance. "Thus, no financial incentives exist for the medical community or the family to cease or reduce treatment and benefits for a patient" (Scherer, 53). In 1981, the Rotterdam criminal court of the Netherlands decriminalized euthanasia in cases meeting the following guidelines:

> [The patient must be] suffering from unbearable pain; the patient must be conscious; the desire to die must be enduring; the decision to die must be given freely and voluntarily; the patient must have been given alternatives to euthanasia and time to consider the alternatives; no reasonable solution to the problem must exist; the death of the patient cannot inflict unnecessary suffering on others; more than one person must be involved in the euthanasia decision; the patient must have a clear understanding of his condition; and extreme care must be taken in actually making the final euthanasia decision. (qtd. in Scherer 56)

Except for the fact that the patient need not be terminally ill, the guidelines seem to protect the patient from a hasty or pressured decision and agree with those set forth by American proponents of euthanasia. With euthanasia allowed only in these cases, perhaps the autonomy and life of every citizen is adequately protected.

However, recent looks at the state of euthanasia in the Netherlands have led to startling realizations. Fears about involuntary euthanasia seem well-substantiated after recent research commissioned by the Dutch government documented that in more than a thousand cases per year, doctors actively caused or hastened death without a patient's request. Herbert Hendin, a New York psychiatrist, visited the Netherlands and interviewed Dutch physicians and public policy planners. He returned shocked "not only at the number of what could only be called wrongful deaths but at the Dutch insistence on defending what seemed indefensible." He claims that the doctors who help set the euthanasia policies are

aware that euthanasia is "basically out of control" (qtd. in Manning 74).

Hendin documents cases that violate every one of the guidelines set forth by the Dutch courts. In one case, a newly diagnosed HIV-positive forty-year-old male without any symptoms is helped to die. In another case, a Dutch court acquitted a psychiatrist who assisted in the suicide of his patient. Her one symptom was depression caused by the death of her two sons and her recent divorce. The court held that that the woman was competent to make the choice, her suffering was "irremediable," and that the doctor was compelled to assist the patient (qtd. in Manning 74-75). Scherer and Simon note that this case is significant, as the Dutch court determined that psychological suffering alone could constitute "unbearable suffering" (60). In another instance, a Dutch medical journal reported a shocking instance of coercion. The case involved a wife who no longer wished to care for her ailing husband. She gave him two options: euthanasia or admission to a nursing home. "The man, afraid of being left to the mercy of strangers in an unfamiliar place, chose to be killed. The doctor, even though he was aware of the coercion, ended the man's life" (Manning 76). William F. May states that the Netherlands, with widespread health coverage, has had problems controlling euthanasia. He asks readers to imagine the potential abuses in the United States "with a population ravenously dedicated to its own quality of life" (qtd. in Manning 71).

Some proponents of PAS have pointed to Oregon's situation as evidence that fears of widespread use of PAS or euthanasia in America are unsubstantiated. Numbers from Oregon have so far revealed a minimal use of the newly legalized option of PAS. In 2001, twenty-one patients chose to end their lives by ingesting a lethal dose of medication prescribed by a physician, accounting for 0.33 percent of the 6,365 Oregon deaths from similar diseases. During 2000, the number was twenty-seven (0.38 percent) of the 6,964 deaths from similar diseases. "The number of Oregonians opting for physician-assisted suicide has remained fairly stable, ranging from sixteen in 1998, the first year the law was in effect, to twenty-seven in both 1999 and 2000" (qtd. in Horsfall 6).

Despite the results from the first few years of PAS in

Oregon, many still hold that the U.S. health care system, in its current state, cannot ethically allow PAS or euthanasia. The serious lack of palliative care, the dearth of adequate psychiatric treatment for depression, and the absence of universal health care create conditions in which the lives of the most disadvantaged are placed at the greatest risk. A 1994 study in the *New England Journal of Medicine* reported that individuals treated at centers serving predominantly minority patients were three times more likely to receive inadequate pain treatment than those treated elsewhere. Additionally, elderly individuals and women were also more likely than others to receive poor treatment (qtd. in NYSTFLL 44). More cause for concern can be found in another study which reported that forty-five percent of patients agreed with the statement, "Good patients avoid talking about pain." This belief was especially found among older patients and those with lower levels of education and income (qtd. in NYSTFLL 46).

Dr. Nicolas Parkhurst Carballeira, director of the Boston-based Latino Health Institute, expresses a crucial concern for those opposing PAS and euthanasia when he says, "In the abstract, it sounds like a wonderful idea, but in a practical sense it would be a disaster. My concern is for Latinos and other minority groups that might get disproportionately counseled to opt for physician-assisted suicide" (qtd. in NYSTFLL 90). Additionally, the NYSTFLL writes:

> Task members felt that no matter how carefully guidelines are drawn, assisted suicide would be practiced the way other medicine in the United States is, that is, 'through the prism of social inequality and bias.' At greatest risk as a result will be minorities, the poor, and the elderly. Cost consciousness can increase the threat that guidelines will be usurped, as doctors, hospitals, insurers, and governments all seek to save money. (vi)

The weighty concerns of Dr. Carballeira and others would have to be allayed before any public policy could be ethically advanced in

favor of PAS or euthanasia. Whether this can be accomplished by PAS and euthanasia proponents is doubtful.

Ultimately, there are only a few public policy options regarding euthanasia and PAS. They are:

1. Ban both PAS and euthanasia in all circumstances.
2. Allow one or both practices in all circumstances.
3. Allow one or both practices, but only under heavy monitoring and restriction.

I believe that a reasoned and comprehensive look at all the factors surrounding the issue supports the current U.S. ban as the only ethical public policy. Though moral philosophers Rachels and Dworkin claim that there is no significant difference between withdrawing treatment and administering life-ending measures, the fact that imposing life-sustaining treatment against a patient's will is similar to battery seems a point strong enough to warrant differentiation. Additionally, the U.S. government, the Catholic Church, and the American Medical Association all contend that a significant difference exists. Furthermore, although allowing only PAS, as is done in Oregon, does protect against cases such as those in the Netherlands in which doctors have ended patients' lives without consent, the option of PAS is still dangerous for such reasons as highlighted by the NYSTFLL, including lack of treatment for those dealing with pain or depression.

Questions of liberty raised by euthanasia's proponents are serious, though I do not believe they can justify the possible consequences of a public policy that allows for euthanasia or PAS. A case could likely be advanced in which all steps to provide care for a terminally ill patient were exhausted, ultimately ending with the patient making a dignified and conscious decision to terminate his life and further suffering. In such a case, denying a patient PAS or euthanasia would cause him harm and a restriction of individual liberty. However, as shown in several studies, pain management and proper treatment for psychiatric problems that come with terminal illness are severely lacking in U.S. medicine. Hence, the ideal case that euthanasia proponents offer is one that is much rarer

than is commonly realized. True, the option to end one's life might be reassuring and even beneficial to some; however, reason suggests that the mere presence of the option could inflict harm on many more. The least advantaged and most vulnerable would be more easily pressured to end expensive care that is sustaining their lives. The mere presence of the option to end life would create the need for a patient to "justify his or her continued existence. The patient will be seen (by others and himself or herself) as responsible for the choice to stay alive, and as needing to justify that choice" (NYSTFLL 95). This easy out could potentially lead the medical community to not fully pursue palliative care with individual patients and may also discourage the pursuit of more effective palliative care in general.

In conclusion, a reverence for life must govern any ethical public policy we wish to advance, and individual liberty must be respected whenever possible. It is admitted by most that when certain conditions are met and all options are explored, it could be preferable for a patient and the patient's family to end a life that is likely to be plagued by continual, unbearable suffering. Moreover, it is recognized that a continued prohibition on PAS and euthanasia will lead to situations where this justifiable action cannot be carried out. However, the number of cases that meet such requirements are far fewer than those in which patients find themselves lacking adequate support and treatment. There are substantial reasons to believe that these disadvantaged patients' lives could be threatened simply because the option of ending life exists. In a time of continually escalating medical costs, such a policy would likely increase the risk of a patient being viewed not as a life to be fought for but as a burden to be cast off. Ultimately, while some liberty may be forfeited by a few, prohibiting PAS and euthanasia best protects the interests and lives of those citizens most often underrepresented and overlooked. Therefore, the public good is far better served by a policy that bans PAS and euthanasia.

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# Analysis of György Ligeti's *Lux Aeterna*

Mary Elizabeth Neal

**Abstract**

The purpose of this paper is to explore the compositional unity found in György Ligeti's *Lux Aeterna*. *Lux Aeterna*, written for 16-part unaccompanied choir, uses a text from the requiem mass, which asks that eternal light and peace be with the dead. Melodically, *Lux Aeterna* is structured through the use of pitch class sets. The piece divides into five major melodic areas in which each section forms a pitch class set. Each major section divides into smaller phrases that, when arranged in normal order and combined with all the sets in that particular melodic area, form the overall set for that section. After identifying the sets, we find that [0123457] and [035] are major structural features in this work. This paper also explores the rhythmic structure of *Lux Aeterna*, which Ligeti called "micropolyphony." This technique consists of layering melodic ideas in close canon at the unison, which creates a seemingly unmetered, atmospheric effect. This paper examines the significance of the text, word painting, and the use of silence as a structural feature. The paper also discusses the importance of this piece in the composer's overall output, and explores the work from the perspective of a performer.

György Ligeti was born in 1923 in Hungary to an artistic family. In his youth, he lived through the oppression of both Hitler and Stalin, and, in 1956, emigrated to Vienna and later Cologne. In 1944, he graduated from the Academy of Music in Budapest and in the following year taught classes in harmony and counterpoint. For much of his compositional life, Ligeti composed choral works in the Hungarian folk style. From 1949 to 1953, a period of totalitarian reign in Hungary made "musical innovation as impossible as political dissent." [1] In 1954, the political hold over Hungary

[1] Paul Griffiths: "György Ligeti" *Grove Music Online* ed. L. Macy (Accessed April 2005), <www.grovemusic.com>

began to dissipate and Ligeti responded with more ambitious and challenging works than he had previously produced. Yet however adventurous his works, he was still limited by his musical experience and exposure, which had been restricted to Bartok and other twentieth-century masters. He longed for a more atmospheric yet structurally complex music. This desire led him to Cologne and the Studio für Elektronische Musik, which was a major center for the avant-garde.[2] The works of Webern, especially the union of highly structured works and extreme expression, influenced Ligeti. At the same time, he was quite aware of the limitations of integral serialism. 1958-1959 brought to fruition his dreams of "unmeasured rhythm, fantastical complexity, and sonic drama"[3] in his orchestral work *Apparitions*.[4]

*Apparitions* and the following orchestral work *Atmospheres* (1961), along with the *Requiem* (1963-1965), pioneer what Ligeti called 'micropolyphony,' which is defined as "dense waves of canons at the unison, in which the lines move at different speeds and are not separately identifiable."[5] *Lux Aeterna*, completed in 1966, is written completely in this mature style. The work for unaccompanied sixteen-part chorus explores tonal centers more than the previous works, but the principle of micropolyphony creates a sound mass that defies tonality.[6]

The text of *Lux Aeterna*, taken from the Requiem Mass, speaks of eternal light and rest. Though there is little evidence of word painting in Ligeti's setting, the text is used in significant structural ways throughout the piece.

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[2] Robert Von Zahn: "Cologne", *Grove Music Online* ed. L. Macy (Accessed April 2005), <www.grovemusic.com>

[3] Paul Griffiths: "György Ligeti" *Grove Music Online* ed. L. Macy (Accessed 2005), <www.grovemusic.com>

[4] Ibid.

[5] Ibid.

[6] Ibid.

| | |
|---|---|
| *Lux aeterna luceat eis* | *Let eternal light shine on them* |
| *Domine* | *Lord* |
| *Cum sanctis tuis in aeternum* | *as with Your saints in eternity* |
| *quia pius es* | *because You are merciful* |
| *Requiem aeternam dona eis* | *Grant them eternal rest* |
| *Domine* | *Lord* |
| *Et lux perpetua luceat eis* | *and let perpetual light shine on them* |

*Lux Aeterna* divides into five major melodic areas. Within each major area, the melody is broken down into phrases according to the text, such as "lux aeterna," "cum sanctis tuis," or "Domine." Each phrase forms a pitch class set, which is then arranged in normal order and combined with the rest of the sets in that particular melodic area to form the overall set. Each melodic area is organized according to the principle of micropolyphony, which here means a very strict melodic canon at the unison with close entrances, much like a stretto.

The opening melody sung by sopranos 1-4 and altos 1-4, as seen below, creates the set [0123457], which is the primary set of the work.

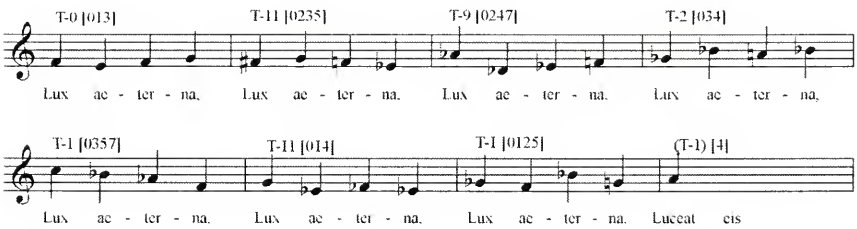


*Figure 1. Primary melody*

Within each of these subsets, all of the chromatic pitches except B and D are used. Soprano 1 and alto 1 reach the final pitch of the opening melody, A, in measure 24, at which point tenor 1 joins. The rest of the voice parts eventually come to the final note by measure 35.

In measure 37, the basses enter for the first time with the text "Domine," and utilizing the set [035]. The extreme register of this section means that the basses must sing in falsetto, producing a lighter and quieter sound. In measure 39, the tenors enter with the text "cum sanctis tuis" using the set [0123457]. This set was derived in the same manner as the A section, with the notes in each phrase taken in normal order as subsets of the larger set. In these transpositions, all chromatic pitches are found except for F and G.

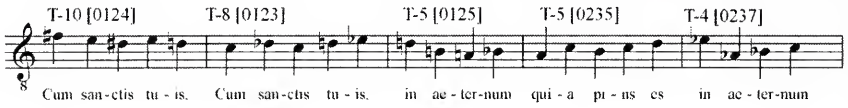


*Figure 2. "Cum sanctis tuis" melody*

This section elides with the C section, continuing through measure 64 in the tenor parts.

At measure 61, the C section begins. This is the first time that all 16 parts have been singing simultaneously, and the texture is suddenly very thick. This section is truly polyphonic, with three melodic ideas occurring at once, and each voice grouping following its own strict canon. The sopranos, on the text "Requiem aeternam dona eis," sing the melody below. The melodic phrases form the set [012345], which is a subset of the primary set.

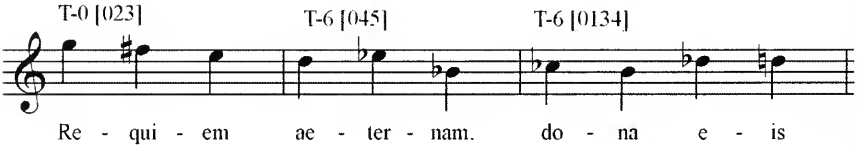


*Figure 3. "Requiem aeternam dona eis" melody*

The altos also sing "Requiem aeternam dona eis" and cyclically rotate through the set [035], relating it to the bass entrance in measure 37.

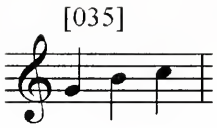


*Figure 4. Alto "Requiem aeternam dona eis" figure*

The male parts sing "quia pius es" using [0234567], the inversion of the original set [0123457].

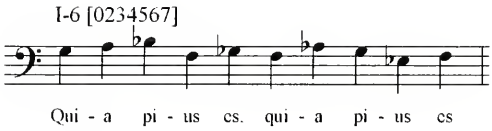


*Figure 5. "Quia pius es" melody*

The women end this section in measure 79, with the sopranos staggering the ending of their final unison D's, and the altos sustaining their [035] cluster chord, GBC. The men's parts, however, continue and overlap with the next melodic section. Beginning in measure 80 with the lowest bass part then building up the score, all male parts enter on the word "Domine" on a unison E. Structurally, this is significant because E is the base note of the T-0 form of the primary set. Once all parts have entered in measure 84, a staggered ending begins in the same manner as the section began, starting with the lowest bass part and moving up the staves. In measure 87, basses 2-4 sing "Domine" in the extreme low register contrasting the extreme high register of the first statement of this text. This statement begins with the [035] set as before, but then contracts and expands the chord, forming the subset [02357].

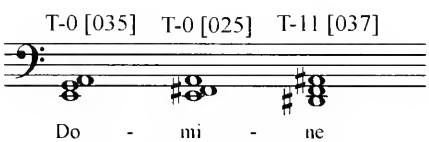


*Figure 6. "Domine" chords*

The last chord of "Domine" occurs at the same time as the alto entrance in measure 90. Through the end of the piece, the altos carry the final melodic material (D section), while the other voice parts provide color by singing sustained tones in extreme registers. The alto melody, on the text "et lux perpetuta luceat eis," uses the subset [012345] in the extreme low portion of their register.

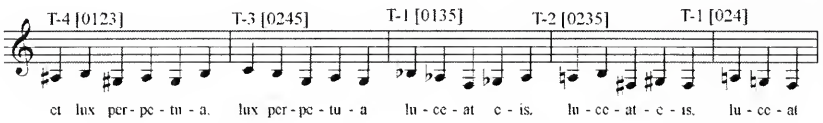


*Figure 7. "Et lux perpetua luceat eis" melody*

In measure 94, there is a final manifestation of the [035] set in the sopranos and tenors. Each part begins on a high B and either sustains or moves down to an A followed by an F#. This set lasts through measure 102. In measure 101, basses 1 and 2 enter on a unison B, followed by basses 3 and 4 on a unison D. These pitches are sustained until measure 114, almost the end of the piece. These pitches are structurally significant because B and D are the aggregate pitches to the A melodic area. The sopranos and the bass 1 enter in measure 110 on middle C. This, with the bass sustained B and D, completes the subset [013]. The sopranos end in measure 114. After the basses end their section in measure 114, the only sound left is the altos sustaining an F and a G, which are the aggregate pitches to the B melodic set. The piece ends with six measures of silence, which at the given tempo marking (quarter note equals 56), is about 30 seconds.

One of the most interesting and puzzling aspects of this piece is the rhythm and, consequently, the texture. In each section of the piece, entrances never align with a downbeat, except for measure 89. This moment is significant because the basses are singing the word "Domine" or God, it is the midpoint of the three-syllable word referencing the trinity, and structurally, it is a turning point in the piece. This obscuring of the downbeat leads to a freer sense of rhythm in this piece, creating a quality of suspended time. Throughout the piece, each voice part deals with a different type of division of the beat.

| Division Level | Voice Parts |
|---|---|
| Regular division/subdivision in 4/4 | Soprano 3<br>Alto 2<br>Tenor 1 and 4<br>Bass 3 |
| Triplet subdivisions | Soprano 1 and 4<br>Alto 3<br>Tenor 2<br>Bass 1 and 4 |
| Quintuplet subdivisions | Soprano 2<br>Alto 1 and 4<br>Tenor 3<br>Bass 2 |

This adds to the free rhythmic feel of the piece by creating the illusion of an absence of definite rhythm, although each voice part is intricately structured to maintain the atmospheric sound-scape and to never coincide with any other part. Despite the complex rhythm that is meticulously laid out, the composer writes "all entries very gentle," and that the piece should be "sung completely without accents: barlines have no rhythmic significance and should not be emphasized." It is clear that Ligeti wanted a sustained sound in which individual lines would not be distinguished.

Ligeti elides the melodic sections of this piece to create seamless transitions and very little silence. For example, in measure 37, as the sopranos, altos, and tenors end the A section, the basses enter in a high register, creating a sense that no one really stopped singing, but merely changed pitches. Also, at the beginning of the C section, the sopranos, altos, tenor 4, and basses enter on the last beat of an eighth-note triplet, while the tenors continue their line into measure 63, smoothing the transition and sustaining the musical aesthetic.

The extreme ranges found in this piece are structural phenomena in and of themselves. The resolution of the first melody on an A is in the upper range of the soprano and tenor voices, and is indicated to be sung *pianissimo*, making it exceedingly difficult to sustain and blend as a choir. The result is a shimmering effect, as the tenors are

singing falsetto and the sopranos must sing with an almost straight tone. The highest note of the piece, found in the soprano and tenor in measure 94 is meant to be sung *piano* and as a background for the alto D melody. The effect is the same kind of shimmering sound as before. In contrast, the extreme lows found in the alto D melody and the final bass "Domine" create a rumbling effect and ground the piece. Extreme range is used as a tool to modify the timbre of the voice to fit the quality of sound Ligeti wanted to hear.

Ligeti's longing for an atmospheric but highly organized sound is achieved in this piece. The "static masses of...sound that give the simultaneous sense of immobility and motion"[7] are the fulfillment of this desire. In writing music that is rhythmically complex, but is perceived aurally as being quite simple but pleasing, Ligeti keeps both the performers and the listeners engaged throughout the piece.

The primary set [0123457], along with its subsets and inversions, brings another level of organization to this piece. While no real melodic motives can be found, the continued use of the set and its subsets brings unity to the piece, especially in the manifestations of the [035] set. This set is used every time the word "Domine" is sung, and is always set in an extremity of the bass range. It is used in the altos as a connective motive in the C section, and is also found in the soprano and tenor as coloration of the final melodic material.

From the aspect of a performer, this piece is extremely challenging, but is also very rewarding. Once the melodic areas are learned and the difficulty of the individual rhythmic lines is overcome, the music truly begins to take shape. The piece is one of great dramatic interest and personal investment - the more a performer gives to this piece, the more he or she receives from it. The six measures of silence at the end of the piece provide a moment for both the audience and choir to reflect on the text of *Lux Aeterna* and allow the sound fade completely from the performance space. It is also possible that the silence at the end of the piece and the silence that generally precedes a live performance act as a frame for the work. The stillness of the ending is a reference to the stillness

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[7] Joshua Cody, "The Ensemble Sospeso: György Ligeti" (Accessed April 2005), http://www.sospeso.com/contents/composers_artists/ligeti.html.

of the beginning unison notes, and peacefully ends the piece which asks for "eternal rest."

## Score used for analysis

Ligeti, György. *Lux Aeterna.* New York: C.F. Peters, 1968.

# Continuing Phoenix's Journey: Social Implications in Eudora Welty's "A Worn Path"

Thelisia Boykin

In "A Worn Path," Eudora Welty tells the story of an old Negro woman, Phoenix Jackson, who travels by foot from her home in the country to the town of Natchez in order to get medicine for her ailing grandson. Welty's description of the obstacles that Phoenix overcomes throughout her journey depicts the profound racial barriers that exist between Whites and Blacks in the story's setting as well as in society at that time. Throughout the South, especially in Mississippi where Welty is from, Blacks were not considered to be equal to their White counterparts. Welty's portrayal of the times is not limited to the incidents that occur during Phoenix's journey; she also carefully selects the words that she uses to describe Phoenix's physical state. Ultimately, Welty weaves these details together to form a critical analysis of the racial climate of that period and its role in the African-American struggle for equality.

I first read this story as part of a class requirement for my eleventh grade literature class. I skimmed through the story haphazardly, highlighting details that seemed important. Later I drew conclusions from those things and completed a fairly good essay. Four years later, I find myself a junior in college in very much the same position. The only difference is that this time, I was able to choose which story I wanted to analyze. I chose "A Worn Path" for many reasons, but primarily because I was interested in knowing whether I would note the same details that caught my attention the first time. After rereading the story, I must say that I am keenly aware of its underlying meaning. Other than my sharpened analytical skills and increased knowledge of events during the Civil Rights movement, I think that it is my unique experience as a Black person at a predominantly White institution that has profoundly shaped my latter interpretation of this story.

Welty begins creating an image of Phoenix, the main

character, by describing her clothing. Phoenix, clad in a dress and apron "reaching down to her shoe tops" (537) with a red rag wrapped around her head, immediately evokes the image of a woman similar to Mammy, portrayed by Hattie McDaniel in *Gone with the Wind*, which debuted around the same time that this story was written. By clothing the main character in such a way, Welty is able to convey that the woman probably does a lot of labor, namely domestic work. This type of work was typical for African-American women during the years following the Civil War and continued throughout the period of the Great Depression. Phoenix's status is further illustrated by the state of her shoes. While she walks, Phoenix's shoelaces are untied to the degree that they might cause her to fall. Aside from the threat of tripping on them, Phoenix is also scuffing them as she walks along the dirt path. I imagine that more than likely, her shoes are so worn that dirtying them further would not detract from their condition.

Phoenix's physical description is also symbolic of the status of Blacks during the late 1930s and 40s. Welty describes Phoenix as having a forehead of "numberless branching wrinkles" (537). All of the wrinkles of her forehead are said to come together to form the base of a tree. Just as a trunk serves as the source of stability for a tree, the same can be said of Phoenix and her role as the guardian of her grandson, for whose medicine she is journeying. The branches are appropriately symbolic of the generations of African-Americans who have persevered for their children. She is paving the way for her descendants; similarly, her family is surviving along side others in hopes of a brighter future filled with more opportunities for Blacks to succeed.

Welty's emphasis on Phoenix's age is a recurring theme throughout the story. She ambles along with a sway that is similar to the "balanced heaviness and lightness of a pendulum in a grandfather clock" as older women tend to do (537). When she realizes that she has mistaken a scarecrow for a person she exclaims, "[...] I too old. I the oldest people I ever know" (539). Later, in an incident with a hunter, he remarks that she "must be a hundred years old, and scared of nothing" (541). When she finally reaches the doctor's office, her conversation with a nurse reveals that she "never did go to school

[...] too old at the Surrender" (542). When all of these details are interpreted together, one begins to contemplate exactly how old Phoenix is. Nancy Butterworth writes, "If we assume that Phoenix was eighteen or more at Emancipation and posit the present action of the story to be around 1940, when it was written, she would be approximately 100 years old" (qtd. in Johnston 227). If this is accurate, her age would have allowed her to bear witness to the debasement of African-Americans from the period before the Civil war leading up to the period before the Civil Rights Movement began (Johnston 227). Perhaps Dennis Sykes puts it best when he writes, "Phoenix Jackson witnesses the Southern black's transformation from slave to citizen" (151).

The capacity of Phoenix's memory is evident in other aspects of her journey as well. As she progresses from the familiarity of the peaceful countryside to the bustling activity of the city, the reader discovers early on that Phoenix's path is one that she knows well when she states, "Seems like there is chains about my feet time I get this far" (538). This is the first time that the story's title, "A Worn Path," is made significant. Physically, a worn path is usually rutted and bumpy due to constant travel. The same is true of Phoenix's; it is worn because Phoenix and many others before her have traveled it so many times. The title also lends itself to a deeper meaning by implying that there may be struggles and discouraging encounters that make it difficult for Phoenix to reach her destination. As I read on, I realized that this was true.

Phoenix faces both natural and human opposition on her path. Phoenix's first challenge is in her natural surroundings. Having made it through the woods unscathed by "wild" animals, such as foxes and coons, waiting to assail her, the path abruptly ends at the base of a large hill. Phoenix states, "Seems like there is chains about my feet time I get this far" (538). The word 'chains' immediately evokes the image of hundreds of African slaves shackled together and stored like cargo in a large ship during the Middle Passage. A more figurative interpretation of Phoenix's struggle to climb up the hill, however, reflects the African-American struggle for equal rights, which led to the Civil Rights Movement. Both Phoenix and later the activists are presented with large obstacles that they must

overcome in order to reach their goals.

Phoenix eventually makes it up the hill, but on her way down, her skirt snags in a sticker bush. As her nimble fingers work at freeing herself, Phoenix states that the bush "Never want to let folks pass," and Phoenix's skirts became so entangled that "before she could pull them free in one place they were caught in another" (538). Each thorn on the bush is representative of the inhibitory laws, influential people, and overall dissention that rendered African-Americans second-class citizens.

Phoenix's human adversaries present her with challenges as well. After leaving the woods, Phoenix encounters a hunter who threateningly warns her that she should return home so that "nothing happens" to her while he aims his rifle at her chest. Baffled by her undaunted expression, the man asks Phoenix why she is not afraid for her life. Stoically, she answers, "I seen plenty go off closer by, in my day, and for less than what I done" (541). As an African-American in Mississippi, it is not so far-fetched to assume that her eyes have seen lynched bodies swaying in the breeze or dragged from a river's depths. It is also plausible that her husband or son suffered a similar fate and that is why she is the person journeying on behalf of her ailing grandson.

When she reaches the doctor's office, the attendant there assumes that she is a "charity case" and acknowledges her as "grandma" (541). These derogatory remarks about her class and age do not cause her to strike out in anger, however; she remains silent and respectful. There is no change in her expression except for a small "twitch to her face as if a fly were bothering her" (542). Either from years of practice or too much exposure to the consequences, she has certainly learned to 'stay in her place' and submit to the desires of Whites who would like to see Blacks remain inferior. The story takes place during Christmastime, and in the 'spirit of giving,' the same attendant gives Phoenix a nickel before she leaves the office. Phoenix decides to use her money to buy her grandson a paper windmill so that he will know "there such a thing in the world" (543). While she cannot give him the opportunity to enjoy the privileges of equal citizenship, she can offer this simple purchase as a way of showing him that there is something more to

attain so that he will continue to persevere in spite of the fact that he may never achieve freedom for himself.

The racial undertones of the story are also apparent in the way that Welty contrasts the colors black and white in the story. The first incidence of this occurs when she describes the colors of Phoenix's dress. Although she describes it simply as being "dark striped," I automatically assumed that it was the colors black and white (537). Following this logic, the colors are alternating, so that each white stripe acts as a boundary for every black one, similar to the way most Whites during that time rebuffed Blacks' attempts to achieve social equality.

Another interpretation of the colors of Phoenix's dress focuses on equality rather than inequality. Rather than interpreting each stripe as a boundary to another, one could argue that their proximity is arbitrary and representative of the contributions that both groups had made to the overall success of society. By taking this view, Welty's decision to make the dress striped is an attempt to recognize that both Blacks and Whites have made invaluable contributions to society. The triumphs and struggles of Blacks and Whites allowed the country to thrive and flourish through continuous advancements, which were aimed at improving the overall quality of life of its citizens.

Regrettably, during this time, most did not consider social equality to be a relevant issue. However, it is likely that each bar in the dress, regardless of its color, has identical dimensions to the one next to it, representing the fundamental similarities that Blacks and Whites share as members of the human race. The only noticeable difference between them was their skin color. Although it was a trivial feature, skin color was the basis for many significant normative customs that were created in order to keep Blacks disfranchised. Considering that these practices were maintained until somewhat recently, it is appropriate to question whether or not their residual effects presently influence society.

The symbolism of contrasting colors is repeated in a dream that Phoenix later has as she rests underneath a tree. In her vision, Phoenix is presented with a slice of marble cake; as she reaches for it, she replies, "That would be acceptable," but she grasps nothing

but air (538). In this instance, the colors black and white are still presented side-by-side. However, this time, they are in a more integrated pattern. In contrast to the stripes of Phoenix's dress, the colors in the cake have a checkerboard effect so that they are broken up into smaller portions. The stripes in Phoenix's dress are representative of Blacks and Whites at the time; they each have their own communities that isolate them from one another. The colors of the cake in the dream are intermingled, depicting the hope that one day Blacks and Whites can really live together as equal members of not only society but also a community. The moment when Phoenix reaches out for the cake and grasps only air symbolizes the empty promises of equality that Blacks had been told throughout the years beginning with Abraham Lincoln's Emancipation Proclamation. That this relationship is being depicted in a dream strengthens the idea that it is still an unrealized hope that many Blacks have for the future. Unfortunately, the actions of Whites are a constant reminder that many still oppose the idea that Blacks and Whites can ever live peacefully together. The probability that this dream may never become a reality is illustrated when Phoenix reaches out her hand to grasp equality but holds air instead.

Because Phoenix is prone to daydreams such as this and incorrect observations due to her poor vision throughout the story, it has been suggested by some that her grandson may no longer be alive. Roland Bartel suggests that if her grandson is dead, her ritual of going to the doctor's office for his medicine has become so much a part of her life that continuing it is her only way of coping with her loss (289). This would also explain her stoicism at the doctor's office because she is remembering her previous visits when her grandson was awaiting her return. In keeping with this line of thinking, it is also logical to assume that the young boy who presents Phoenix with a piece of marble cake in her dream is in fact her grandson. To imagine that he would present her with something, anything to make her long journey worthwhile, is simply a reminder of the joy that he once brought to her life. Although a plausible explanation, I do not believe that this is indeed the case. Welty herself writes,

As the author at one with the character as I tell it, I must

> assume that the boy is alive. As the reader, you are free to think as you like, of course: The story invites you to believe that no matter what happens, Phoenix for as long as she is able to walk and can hold to her purpose will make her journey. ("Phoenix Jackson's Grandson" 604)

Regardless of whether or not her grandson is indeed alive, the focus of the story is Phoenix's perseverance along her journey and its implications about her character. Consequently, the symbolism of her journey extends to a representation of the journey toward equality that all African-Americans at the time were making.

Finally, Phoenix's name creates an element of mysticism as well. The connotation of the mysterious bird that rose from its ashes to live again is apparent not only in her name, but in her determination to finish her journey (Seidl 53). Welty writes, "Of course I knew what that meant when I named Phoenix Jackson, but it was also a name that was common among old black women. . . poor people in the South tend to give their children beautiful names. They think, 'Well at least I can give her a pretty name.' And they do" (qtd. in Ascher 84).

Having reread "A Worn Path" with the knowledge that I have gained from my life experiences, I more fully understand Welty's efforts to portray the time in which she lived. My experiences have also allowed me to better appreciate the story's overall significance. The time that I have had to grow as an individual has allowed me to gain greater insight into the way people think. Over half a century after "A Worn Path" was written, I realize that things are not so different today. Although Black people have made a lot of social advancements, there are still subtle boundaries that prohibit Blacks and Whites from being fully equal. I am a minority on this campus and my experiences at Birmingham-Southern have taught me that whether I like it or not, I am held to a higher standard. For many who have had limited contact with African-Americans, I am a reference, in their later encounters, for how a typical African-American behaves. To others, I may be a pundit on the inner workings of my race.

There are times when others' insights are not as insightful as

they should be, but like Phoenix, I am not permitted to mirror their thoughtlessness. Because I have the opportunity to impact their perception of Black people in general, it is my duty to represent my race and myself with poise. My skin color, the very thing that alienates many from knowing the person who lives within it, is my badge of honor. However, I cannot remove it. I wear it proudly as I walk to and from my classes, but this is not always easy. One thing that I have learned from being here, though, is that as difficult as it is for me to deal with it, it is oftentimes just as difficult for those who outnumber me. Some are unsure about whether or not I am secretly hostile and do their best to maintain my good cheer while others could not care less if I had ever entered their presence. Still there are others, whom I believe to be the majority, who are simply unaware of their feelings toward Blacks until I help them realize. Yes, I recognize that it is both a burden and a privilege to be Black. The power to change minds is a large responsibility bestowed to the few who are willing to undertake the task.

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# The Tennis Racquet Industry

Marcus Dillender

## Introduction

Tennis started about 900 years ago in France and has not stopped growing since then. Because racquets were not used at the time, the first tennis players would be surprised that the industry for tennis racquets has grown to be as large as it is today. In 2002 alone, revenues for all of the racquet-producing firms combined were over $900,000,000 (6). As with any industry, technology, consumers' tastes, and the state of the economy in general has affected and continues to affect the market for tennis racquets. Many factors are involved with the selling of tennis racquets that actually do not have anything to do with tennis racquets but still garner much attention from those involved in the industry.

## The Basics of the Good

### Luxury Status

The nature of tennis racquets has caused the tennis industry to be largely unregulated. The tennis racquet is a luxury good and a sudden adverse supply shock of tennis racquets would not greatly hurt the economy or threaten national security. Nobody needs a tennis racquet for his or her everyday functions. Tennis racquets are not inputs for other goods or necessary for business. This keeps the industry from being as closely scrutinized as an industry such as oil.

### Substitutes and Quality Discrimination

There are no close substitutes for tennis racquets. Although some people may decide not to play tennis if the price of racquets becomes too high, there is not a way to play tennis without a racquet, which means that if people want to play tennis, they must purchase racquets from one of the major manufacturers. People do not use racquetball racquets or badminton racquets in lieu of tennis racquets. Racquets do vary greatly in price. The average price of a racquet sold at a chain store is $50 while the average price paid at a specialty store is much higher (3). So while there

are no substitutes for the tennis racquet, there are substitutes for the higher-quality racquets, which is why most of the big manufacturers make a variety of racquets that range greatly in price. To a degree the manufacturers practice quality discrimination. There are really low quality racquets and really high quality racquets with few in the middle. If a consumer wants a decent racquet but not a spectacular one, he will still have to buy the spectacular one and pay a high price.

Any other sport is a substitute for tennis to a certain degree. People can play a wide variety of sports, which means that tennis has to compete with all of them to assure that the demand is high for tennis equipment. While other sports are substitutes for tennis, tennis faces stiffer competition from passive activities (11). The rest of the entertainment industry, not solely the other sports, takes people away from tennis. People may not start playing tennis because it is too expensive, but few people who already play will readily switch to another sport if the prices rise a little; they might instead buy bargain equipment. This means that tennis has a relatively inelastic demand among those people already playing.

**The Cost of a Game of Tennis**

The tennis racquet is a fixed cost and is the most expensive part of playing tennis. Once it is purchased, the marginal cost for each additional game is relatively low. This is because the variable costs, such as court fees and balls, are low. Some people may not be able to purchase a racquet, but once someone does, tennis is not nearly as expensive. The demand is becoming more elastic as the game continues to grow in popularity among lower income people (12). People with less money will be more sensitive to changes in the prices.

Structure

**The Companies**

The three main manufacturing firms in the industry are Wilson, Prince, and Head. Wilson is the leader with about 35% of the market (5). Wilson used to have even more of the market share, but in recent years Prince and Head have gained on it. Head became second in the market after it passed Prince due to its introduction of the titanium racquet. The market is relatively volatile because

if one firm can get one popular racquet, its revenues will be much higher than normal. Babolat, Dunlop, Estusa, Fischer, ProKennex, Slazenger, Volkl, and Yonex are the other firms in the market, which gives it a total of eleven firms. While tennis racquets bring in the most revenue for these companies, some of them, such as Head, Prince, and Wilson, are involved in other sporting industries too. Wilson is a subsidiary of a much larger corporation, the Amer Group, which has its roots in the cigarette industry (6). Amer Group purchased Wilson in 1986 and during the 1990s caused it to become one of the biggest sporting goods manufacturers (13). Prince makes racquets for squash and badminton as well as tennis (14). It has diversified into tennis clothing more than most other firms; in fact, before it was purchased in 2003 by Lincolnshire Equity Fund, it was a part of the clothing company Benetton (14). Head makes winter gear and equipment for diving in addition to tennis (15).

**Organization**

While the firms in the industry do occasionally work together, there is no evidence that they have colluded to restrict quantity and therefore increase price. The industry seems to be a cross between an oligopoly and a monopolistically competitive market. The product differentiation makes it seem more like a monopolistically competitive market, but there are barriers to entry, such as name recognition and high start-up costs, which make it seem more like an oligopoly. Being bigger is better in the tennis industry because of economies of scale. Getting racquets shipped to all of the retailers and adequately studying the industry requires a large organization with vast resources. Each firm has several different tennis racquets on the market because if one firm starts making a lot of money with one type of tennis racquet, other firms will start making a similar racquet to get some of the profit while continuing to make the ones that they made before. This has happened in the past when Dunlop introduced long-body racquets. The popularity for these racquets was so high that soon every manufacturer offered multiple long-body racquets. This happened again when Head introduced racquets with titanium and other companies soon followed.

**Rectifying the Free Rider Effect and Increasing Participation**

If sports are viewed as goods, then racquets can be seen as a complement good for tennis. People in the tennis industry know this, which is why they do what they can to increase the demand for tennis. Taking actions to increase the demand for tennis helps all of the makers of tennis equipment, yet there is probably not as much of this as would best help the various manufacturers and retailers. The reason for this is that everybody benefits from increasing the demand for tennis, even the firms that did not put much money into the effort. Free riders can gain the benefits from increasing the demand for tennis without the costs associated with it. To rectify this problem, the various groups from the tennis industry, from retailers to manufacturers of all tennis related products, have joined together to form the Tennis Industry Association, whose goal is to increase the demand for tennis. The TIA and the United States Tennis Association (USTA) sponsor free tennis lessons all over the country (2). They have recently set up Tennis Welcome Centers designed as places where people who do not understand the game can go to learn about it (6). These centers will have everything that beginners need to play the game. Increasing the demand for tennis will increase the demand for all of its complements. Tennis manufacturers and retailers are in a position in which it is not enough merely to fight each other for market share. They need to increase the total number of people playing the sport, which may be even more beneficial than just getting a higher market share; after all, half of 50 is less than 20% of 200.

The tennis industry has targeted the various demographics in different ways. Young children make up one group that the tennis industry is trying to utilize (9). The TIA has made commercial advertisements that promote tennis that air on the Cartoon Network, TNT, and TBS (9). However, the population of people playing tennis is aging (11). The percentage of people who play that are over 35 increased from 29% to 43% between 1995 and 2001 (11). While this could mean that a lot of people over 35 have suddenly become interested in the game, this is unlikely. It is more likely that tennis has stopped attracting as many young people over the past decade as it had in the previous few. One possible reason that fewer young people play tennis is that physical education is being taken out of the

school curriculum. According to the president of Wilson, this will cause the demand for all sports to fall because people will have less of a desire to be physically fit (4). Another age demographic that the TIA is targeting is elderly people. It has recently teamed up with the American Association of Retired Persons (AARP) to try to get more players over the age of 50 playing tennis (10). To do this the TIA and the USTA have begun hosting free tennis parties (10).

Recently, more women have become involved in tennis (11). This is probably due to several things. The first is that there is a general increase in how many women want to play sports. This can be attributed to several things, one of which is Title IX. Title IX is a law that was passed in the 1970s to assure that women were given equal opportunities in sports. Although the law has been controversial, it has successfully increased women's participation in sports. Another reason that more women are playing tennis is related to how the tennis industry has been marketing tennis. The tennis industry has tried to differentiate itself as the sport that females can play while maintaining their femininity. There have been ads that show women being savage and brutal during a point but coy and innocent after it is over.

**Conduct**

**Retail**

The retailers comprise a much more competitive market than the manufacturers do, which causes them to have less bargaining power over the manufacturers (12). If one retailer will not give in to a manufacturer's demand, the manufacturer will go elsewhere. The retailer needs the manufacturer more than the manufacturer needs the retailer. Currently, most people buy racquets at specialty stores or superstores. There are large amount of both of these. The increased competition causes economic profits to be lower for retailers than for manufacturers. The retailers cannot compete on product like the manufacturers can because the retailers all sell the same things. The manufacturing firms give the retailers a suggested retail price. The retailers usually sell the racquets at this price so retailers have to look for other ways of competing (12). One of the main ways that retailers compete with each other is on customer service (12). Having good salespersons is important to them. Retailers also do

what they can to make sure their name is remembered. One way they do this is by putting stickers on people's racquets; these stickers function as free advertising (12).

The retailing aspect appears to be dominated by superstores more than it has been in the past (9). The superstores sell a broad range of goods, sporting and otherwise, while specialty tennis stores focus solely on tennis equipment. This means that people can purchase racquets cheaper from these superstores than by going to a specialty store, but in doing so they sacrifice the advice that they could get from the experts that are at specialty stores. This advice is especially important for somebody new to tennis because racquets are customized to match people's preferences and body sizes. These customizable options include grip size, string tension, racquet length, and racquet head size. The specialization by specialty shops allows them to be the most knowledgeable but the racquets cost more when bought from these places.

**Warranties**

Most of the manufacturing companies offer warranties for the more expensive racquets and thus commit to providing a service for the duration of the warranty. There is a moral hazard associated with supplying warranties, which can hurt the manufacturers. People are less cautious with racquets if they know they can get a brand new racquet if something happens to their current one. For instance, people will leave them in hot cars for longer, which makes them more likely to break, or people might be more likely to hit them against the ground. Even though such actions are not covered under the warranties, it is usually not possible to tell if a fracture on a racquet was caused by the racquet being slammed against the ground or by hitting a ball.

**Capitalizing on other Sectors of Tennis**

Many tennis racquet firms produce accessories as well, such as grips, string, and other novelty items, which serve as complements for the racquets. By controlling many sectors of the tennis industry, firms can increase the profits made from selling racquets, which brings in more revenue for them. For example, while Prince is currently third in market share for racquets, it is the leader in the market for balls. A lot of these goods come "free" with the racquets,

making them tie-in goods. String is an example of this. Retailers often offer a "free" string job with the cost of the stringing being added to the price of the racquet. Increasing the demand for tennis racquets causes the demand for the other products to rise, but the relationship is not nearly as strong going the other way. People will not buy a new racquet just because the price of grips gets cut in half, while more grips would certainly be bought if the price for a racquet was cut in half. Although part of this has to do with the fact that their respective prices are so different (half off of a tennis racquet is a lot more than half off of a grip), part of it is probably due to the fact that the cross-price elasticity of demand for racquets relative to the demand for grips is much more elastic than the cross-price elasticity of demand for grips relative to the demand for racquets, which is highly inelastic.

**Technology**

The problem that manufacturers are currently facing is that there are not many more ways to improve the racquet, and if there are, they will not be revolutionary improvements that drastically increase sales. The improvements over the past few decades have been minor and have progressed gradually. Not since graphite racquets replaced wooden racquets has something come along that has really grabbed people's attention and made people who were not already tennis players want to try it and people who had the old racquet think that they needed the new one (1). People will continue to use their current racquets for longer if the new ones on the market are only slightly and almost unnoticeably better the old ones. In 2001 a little less than 40% of new racquets were purchased with the intention of improving a player's game (11). If the industry can persuade more people to buy new racquets to help them play better, everyone involved will be better off. The fact that the tennis industry has not been able to increase demand much has helped to cause the prices for tennis racquets to compress over the past several years (8).

The minor improvements are still important in dividing the market share among the various manufacturers, even if big innovations have not been drastically increasing total sales of racquets. In 1997 Head introduced titanium racquets, which were

made of less than one percent titanium (1). One of them became the top-selling racquet in the industry and allowed Head to move past Prince into the number two spot for market share (1). This caused the other manufacturers to have to innovate or continue to suffer losses in profits. To get back some of the market share that it had lost, Wilson sought something that would outdo Head's titanium racquets. After a lot of research, it came out with a racquet made from technology used by space programs (1). The racquet, which was called a hyper carbon, was extremely light-weight and met with instant success when it was introduced to the market. Pro Kennex increased its market share by using Kinetic technology (3).

Technology's importance extends beyond the actual racquet itself. As firms look to cut costs and increase their profits, they are increasingly turning to machines to aid in the manufacturing process. For example, Head has robots that sand racquets after they have been molded, and others that paint and decorate racquets (1). Robots are more efficient and cheaper than labor. As the marginal product of capital continues to increase relative to labor, companies will buy more capital and hire fewer workers.

**Wilson's Strategies**

Before Head's introduction of the titanium racquet, Wilson had 50% of the market (4). The reason that it was able to get such a high market share was because of the marketing strategies it used. Instead of spending as much money on advertising, it devoted its efforts to simply focusing on what the average player wanted (4). Its goal was to fulfill consumers' needs and not to create them (4). This is not to downplay advertising's importance, which will be discussed later. Wilson also maintains close relationships with tennis instructors, which has helped Wilson since the instructors are often responsible not only for helping people decide which racquet to get, but also for selling it to them (4). The president of Wilson, Jim Baugh, had the plan of having Wilson employees work as closely with the consumers as possible. To do this he eliminated much of the corporate staff (4). He did not see a need for the corporate staff so he eliminated it. Cutting extraneous costs allowed Wilson's profits to increase.

**Differentiating the Products**

When it comes to the tennis racquet industry, small differences alter how many racquets of a certain type get sold, which is why manufacturers take great care with product differentiation. The differences between their products are quite small, yet the manufacturers advertise as though they are highly important. Tennis is a cross between a search good and an experience good. People can hold a racquet and examine it in the store. They can see how light it is and how big the frame is. These characteristics make racquets seem more like search goods. Consumers cannot tell how the racquet feels when playing until after they purchase it. They will only know how a racquet has been marketed or what they have heard others say about it, which makes it more like an experience good. Its having the qualities of an experience good means that the consumers do not have full information about which racquet would be best for them. One way of rectifying this is through trying out demo racquets, which most specialty stores have available. This is a form of screening, which is a way that the uninformed party can become informed.

**Advertising**

Although screening helps make consumers aware of what a racquet is like, it does not fully resolve the lack of information on their part, which heightens the importance of advertising for firms. Consumers have to pay more attention to the advertisements because they have few other options on which to base their decision of which racquet to get. Most of the advertising for tennis racquets is a mix between persuasive and informational. Manufacturers are usually the ones doing the advertising. The facts about their product that they have in their advertisements are informational, but the advertisements usually involve a professional tennis player. The idea of doing this is to make people think that they will play like the professional if they have the racquet. Companies pay out large sums of money to get professionals to use their equipment. It is difficult to tell sometimes what the legitimate differences between racquets are. Sometimes the companies use spurious differentiation in their advertising. The titanium in Head's racquets was believed by some people to be so small that it made no significant difference in the

racquet's performance (1). Head marketed it in a way that revealed it as the newest and best thing in racquets. It put a window in the racquet allowing people to see the titanium inside and painted it silver to remind people of the metal inside it (1). The manufacturers do not advertise on price. Doing this would cause prices to be lower, which would help the consumer but hurt the firms.

Conclusion

Various factors affect the performance and the structure of the tennis racquet industry. It is interesting that companies that sell products that have such little differences between each other can have a wide disparity in market power. This reveals the importance of marketing and advertising in the industry. Like many industries, the tennis racquet industry is highly cooperative; however, unlike other industries, the firms involved with tennis have to cooperate with each other in order to survive. Their cooperation does not manifest itself in the form of higher prices and reduced output. They have worked together to try to increase the total number of people who play tennis. A decrease in the sport's popularity is their greatest threat.

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# Identification of *Saccharomyces cerevisiae* strains that are resistant to HePC due to PDR and LEM3 mutations

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Abstract

The purpose of this experiment was to identify and characterize HePC resistant strains of *Saccharomyces cerevisiae*, which did not have PDR or *LEM3* mutations, in order to gain more information that could be applied to the problem of cancer cells resisting drugs. Wild-type yeast cells were mutated using the base-modifying chemical EMS and grown on SDC+HePC to select mutants. Plasmid complementation was performed to determine whether or not the mutants carried hypomorphic alleles of *LEM3* that could make the yeast resistant to HePC but not other drugs. MIC assays were performed on strains with inconclusive plasmid complementation results. A transactivation assay was performed to test if the HePC resistant strains carried hypermorphic mutations in *PDR1* or *PDR3*. The strains were additionally tested for PDR mutations by growing them on plates with cycloheximide to see if they were resistant to other drugs. Fluorescence microscopy was performed on strain HW to determine if it had normal lipid uptake.

Mutant strains MB2, RS, and KM were found to be *LEM3* mutants. Strain MM appeared to exhibit a PDR mutation because it was resistant to cycloheximide. The transactivation assay had uncertain results, but it appeared that strains TA, HW, MB, HG, and JG were not PDR mutants. Strain HW was further tested with fluorescence microscopy; it appeared to have normal lipid uptake, so its mutation was probably not due to a *PDR1*, *PDR3*, or *LEM3* mutation. Since the HW strain seemed to attain drug resistance by a mutation other than a change in *PDR1*, *PDR3*, or *LEM3*, and previous testing showed that it was not a dominant mutation, HW would be a good candidate for further characterization by DNA sequencing. In addition, strains TA, MB1, HG, and JG also may have novel mutations.

## Introduction

A major problem encountered by researchers in their attempts to destroy cancer cells is the ability of the cells to mutate in ways that make them resistant to drugs. These resistant cells multiply, and the drug quickly becomes ineffective. Therefore, researchers must learn about possible mutations in order to create a drug that can kill these newly resistant cells.

The goal of the experiment was to identify and characterize mutant yeast strains that display resistance to hexadecylphosphocholine (HePC), an anti-cancer drug. HePC is a type of alkyl-lysophospholipid (ALP) that can induce apoptic cell death in tumor cells (Ruiter 1999). In these cells, one or more different mutations may prevent the drug from inhibiting intracellular targets that the cell needs to survive. Evidence suggests that HePC inhibits protein kinase C and is competitive with phosphatidylserine (Uberall 1991). The cell could have a mutation that causes overproduction of the intracellular target or alters the shape of the target (Hallstrom 2001). Overproduction would mean that the cell continues to have working targets even after the drug has bound, and altering the shape would prevent the drug from binding to inhibit the target.

The cell can also have mutations that affect the accumulation of the drug. Accumulation can be reduced by either preventing the drug from entering the cell or pumping the drug out of the cell. *ERG6* within the plasma membrane can prevent the lipid-like drug from entering the cell (Emter 2002). The transporter PDR5p works in the plasma membrane to pump the drug out of the cell (Cadek 2004). Other mutations include compensation for the effects caused when the target is ineffective, disruption of enzymes from converting the inactive form of the drug to the active form, and degradation of the drug before reaching its target.

A mutation causing resistance to other drugs is known as pleiotropic drug resistance (PDR). PDR is often caused by hypermorphic mutations in either the transcription factor *PDR1* or *PDR3*; they bind to enhancer elements and increase transcription of the *PDR5* gene. This increases the number of Pdr5p drug pumps. Mutations in transcription factors can be identified by measuring

the products of the gene being transcribed; this can be accomplished through a transactivation assay that measures an easily identifiable product.

Since PDR is a dominant trait, another explanation is necessary when cells exhibit resistance to HePC as a recessive trait or are not resistant to multiple drugs. Cells which are not resistant to cycloheximide may have inactive *LEM3*. Active Lem3p is necessary to prevent HePC from entering the cell, and although Lem3p does not confer resistance to cycloheximide and some other drugs, cells without active Lem3p become hypersensitive to the drug (Hanson 2003). *LEM3* mutations can be identified with plasmid complementation. When a normal *LEM3* gene is added to mutant *LEM3* DNA, the cell becomes HePC sensitive again.

The goal of this experiment was to identify and characterize strains of *Saccharomyces cerevisiae* that have mutations leading to HePC resistance that are not due to changes in *PDR5* or *LEM3*.

Materials and Methods:

Cells that had previously undergone mutagenesis were examined to determine if they possibly displayed novel mutations to HePC. The cells were streaked on SDC+HePC plates to ensure that they were resistant to the drug. The cultures that were resistant to HePC were retested for LEM3 and PDR mutations through plasmid complementation and transactivation assays. The yeast media (YPD) used was made according to standard methods (Sherman 1979). YPG, SDC-ura, SDC-ura+HePC, PHY3 (MATα$his^{+}lys^{-}ura^{-}$), and PHY2 (MATα$his^{-}lys^{+}ura^{-}$) were also made according to previously described methods (Katzmann 1994).

Plasmid Complementation

Cultures of each mutant strain were grown in separate sterile tubes with 3mL of liquid YPD and placed in a 30°C shaking water bath the day before the lab. On the lab day, the culture was vortexed, and 1mL was placed in two microfuge tubes. The tubes were placed in a microfuge for one minute at 13,000 rpm. The media was removed, the pellets were resuspended in 500ul of sterile distilled water, and the tubes were microfuged again. The water

was removed and the pellets were resuspended in 200ul of 100mM lithium acetate. The cells were spun, and the lithium acetate was removed. The pellets were resuspended in 200ul of 100mM lithium acetate again, the cells were spun, and the lithium acetate was removed. 240uL of 50% w/v $PEG_{3350}$, 36 ul 1.0M lithium acetate, and 25 ul of 2mg/mL carrier DNA were added to the tubes. 50ul of plasmid DNA (pGFP-N-FUS::*LEM3*) were added to one tube, and 50ul of empty vector (pGFP-N-FUS) were added to the other tube. The tubes were vortexed for 1 minute, and incubated at 30°C for 30 minutes. Then the cells were heat shocked in a 42°C water bath for 20 minutes. The tubes were microfuged, and the supernatant was removed. The cells were resuspended in 1mL sterile water, the tubes were microfuged, and 800ul of water was removed from each tube. The cells were resuspended, each sample was plated on its own SDC-ura plate, and each sample was incubated at 30°C for 3 days.

Two transformed (*LEM3*) colonies and two empty vector colonies were streaked on a SDC-ura+HePC plate. A known transformed (*LEM3*) colony and a known empty vector colony were streaked on a SDC-ura+HePC plate. These plates were incubated at 30°C, and the growth was recorded on the BioDoc-It system two days later.

MIC Assay

To perform the MIC assay, 300ul of culture was added to 2.7ml of SDC and vortexed. Then the absorbance was recorded at 575nm using a spectrophotometer and multiplied by 10. 1ml of suspension was made up to have an absorbance of 0.1 by using the equation $C_1V_1=C_2V_2$. 0.5ml of this diluted solution were added to 9.5ml of SDC and used in a dilution series (starting with 100ul SDC and 100ul of HePC) in a microtitre plate.

Transactivation Assay

This assay was performed in the same manner as the previous transformation. However, only one tube was used and the plasmid DNA was PDRE-α-gal instead of pGFP-N-FUS::*LEM3*. After growing for three days on the SDC-ura plate, the plate was placed in the refrigerator. Three liquid SDC-ura colonies were started the day

before the next portion of the assay was performed.

2ml of fresh SDC-ura were added to each culture four hours before the experiment began. Then 300ul of *pdr3-11* culture was transferred to a separate tube. 2.7 ml of SDC-ura was added, and the mixture was vortexed. The "red" Spec20 measured the absorbance at 630nm and 3ml of SDC-ura was used as the blank. The reading was multiplied by 10 and recorded.

Next, 1ml of the original *pdr3-11* was transferred to a tube, centrifuged for 1 minute at 13,000 rpm, and the supernatant was carefully removed. The sample was resuspended in 1ml of Z buffer, and the suspension was transferred to a glass test tube. 1ml of Z buffer was added, and 2ml of Z buffer was added to another tube to be used as a blank. 6 drops of chloroform and 4 drops of 1%SDS were added to each tube. Then the tubes were vortexed at top speed for 10 seconds and incubated at 28°C in a water bath for 5 minutes. The tubes were returned to the chemical hood and 0.4ml of ONPG in Z buffer was added to each tube. The tubes were vortexed for less than a second, and a timer was started to record the amount of time needed for the reaction to occur. The tubes were incubated at 28°C until the liquid turned a pale yellow color. The reaction was immediately stopped by adding 1.0ml of 1.0M $Na_2CO_3$. The tubes were gently shaken, and the elapsed time was recorded. The absorbance was recorded for 420nm in the "blue" Spec20. The activity in α-gal units was recorded.

This procedure was repeated, without creating more blanks, for two more samples of *pdr3-11* yeast, 3 samples of wild-type yeast, and 3 samples of mutant yeast.

Cycloheximide Resistance

PHY2 (a wild-type haploid strain) and PHY3 (a HePC resistant haploid strain) were grown on a cycloheximide containing plate as controls at 30°C. Haploid mutant strains TA, MM, and HW were also grown on plates containing cycloheximide at 30°C. The growth of the plates was recorded on the BioDoc-It system.

Fluorescence Microscopy

Lipids were prepared by dissolving phospholipids in

chloroform and dried under a stream of nitrogen. The lipids were then resuspended in DMSO. 20ul of this stock was added to 1ml of the wild-type strain (PHY2) and incubated in a shaking water bath set to 30°C for 30 minutes. Then two volumes of ice-cold SC-azide were used to wash the cells 3 times. The cells were then analyzed using fluorescence microscopy. This process was repeated with the HW mutant strain.

Results:

Figure 1 shows the growth of HePC resistant mutants that are known to have a *LEM3* mutation when they have been transformed with a *LEM3* containing plasmid (pGFP-N-FUS::LEM3) or empty vectors (pGFP-N-FUS) and streaked onto a SDC-ura+HePC. The known *LEM3* mutant grew when transformed with the empty vector, but it did not grow when transformed with *LEM3*. It also shows the growth of mutant strains with unknown mutations that have been transformed with *LEM3* (*LEM3*) and empty vectors (fus) on SDC-ura+HePC. When MB2, RS, and KM were transformed, the cells transformed with *LEM3* did not grow as well in the presence of HePC as the cells transformed with empty vectors. This transformation was performed to check for plasmid complementation that would prove that the cells had *LEM3* mutations.

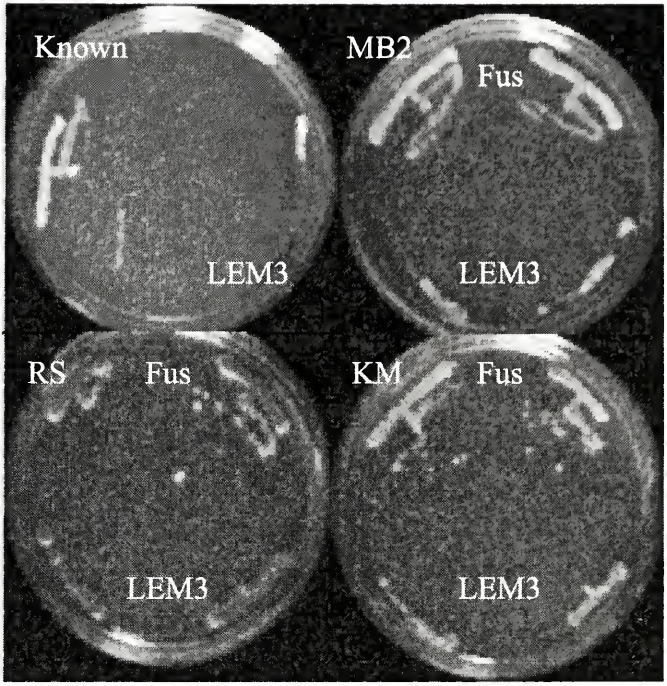
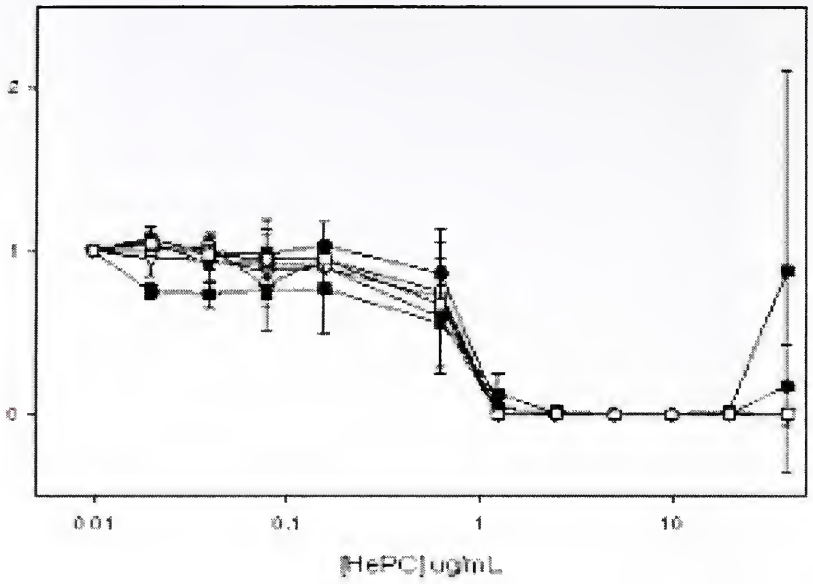


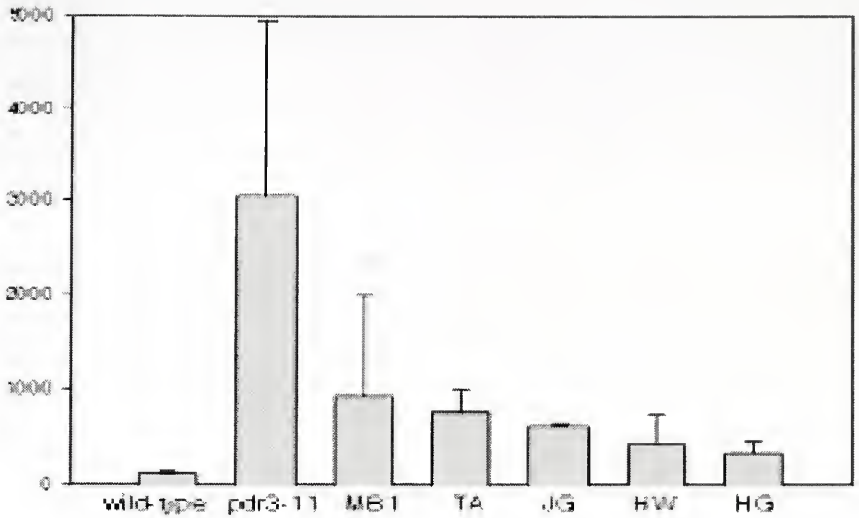

Figure 1: Plasmid complementation. "Known" represents the growth of known *LEM3* mutants when transformed with empty vector plasmids (Fus) and *LEM3* plasmids (*LEM3*). MB2, RS, and KM are HePC resistant strains with unknown mutations that were also transformed with empty vector plasmids (Fus) and *LEM3* plasmids (*LEM3*).

Graph 1 shows an MIC assay performed on mutant strains JG, HW, and HG that were previously transformed with empty vectors (pGFP-N-FUS) and *LEM3* (pGFP-N-FUS::LEM3). This assay was performed in order to determine if a *LEM3* mutation was present by observing the effects of different concentrations of drugs on the cells. All three strains showed reactions to HePC that were similar whether they were transformed with empty vectors or with *LEM3*.




Graph 1: MIC assay of HePC resistant strains JG, HW, and HG. Circles represent JG, triangles represent HW, and squares represent HG. Colored symbols indicate strains transformed with empty vectors (pGFP-N-FUS), and open symbols represent strains transformed with *LEM3* (pGFP-N-FUS: :LEM3). The strains reacted similarly to HePC, whether they were transformed with empty vectors or *LEM3*.

Graph 2 below shows the ß-galactosidase activity of wild-type, *pdr3-11* hypermorphic mutant, and HePC resistant strains (PHY2 mutants MB1, TA, JG, HW, and HG) of yeast when they have been transformed with *PDRE* ß-gal. The HePC resistant mutants displayed less than 1,000 ß-galactosidase units of activity, the wild-type had expression of about 100 ß-galactosidase units, and the *pdr3-11* strain had significantly higher ß-galactosidase units ranging between 3,000 and 5,000. This transformation was performed to determine the level of transcription activity by measuring the amount of ß-gal produced.




Graph 2: ß-galactosidase expression when strains are transformed with *PDRE*-ß-gal. Wild-type yeast had ß-gal activity of about 100 ß-galactosidase units, *pdr3-11* had ß-gal activity ranging from 3,000 to about 5,000 ß-galactosidase units, and the MB1, TA, JG, HW, and HG mutants had ß-galactosidase activity that was below 1,000.

The T-test in Table 1 was performed to determine whether or not significant levels of difference were found between the ß-galactosidase units of the wild-type strain and the ß-galactosidase units of the mutant strains. P values less than 0.05 indicate significant difference. Only the ß-galactosidase units of strain MB1 showed insignificant differences from the ß-galactosidase units of the wild-type strain.

| Mutant Strain | P value compared to wild-type strain | Trials |
|---|---|---|
| pdr3-11 | 0.0013791336 | 7 |
| MB1 | 0.063485086 | 3 |
| TA | 0.0000537049 | 3 |
| JG | 0.0000009601 | 2 |
| HW | 0.0139566026 | 2 |
| HG | 0.0011107811 | 2 |

Table 1: T-test of mutant strains compared to ß-galactosidase units of the wild-type strain. The P values were influenced by the number of trials of the transactivation assay. P values less than 0.05 indicate significant difference. Only strain MB1 had insignificant differences to the wild-type strain.

Figure 2 shows *Saccharomyces cerevisiae* grown on a plate containing the drug cycloheximide in order to determine if strains MM, TA, and HW exhibit PDR. PHY2 and PHY3 were grown as controls; neither grew in the presence of cycloheximide. TA and HW did not grow well with cycloheximide; MM, however, grew well in cycloheximide's presence.

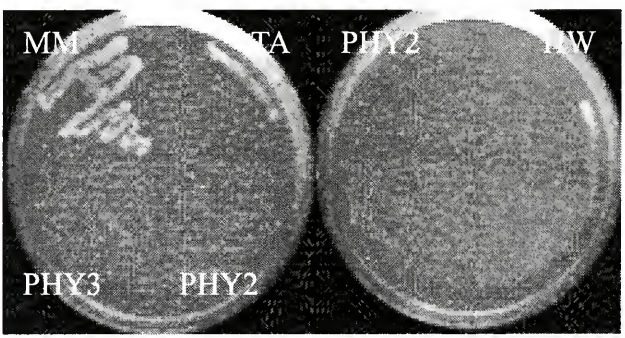



Figure 2: Cycloheximide plates. Three HePC resistant strains of *Saccharomyces cerevisiae* (MM, TA, and HW) were grown on plates containing cycloheximide. PHY2 and PHY3 were grown as controls.

Figure 3 below shows the wild-type (PHY2) and the HePC resistant mutant strain HW when viewed under a microscope using differential interference contrast (DIC) and under a fluorescence microscope (NBD-PC). The level of fluorescence indicates the lipid uptake of the cells. The wild-type and HW mutant exhibit similar levels of fluorescence.

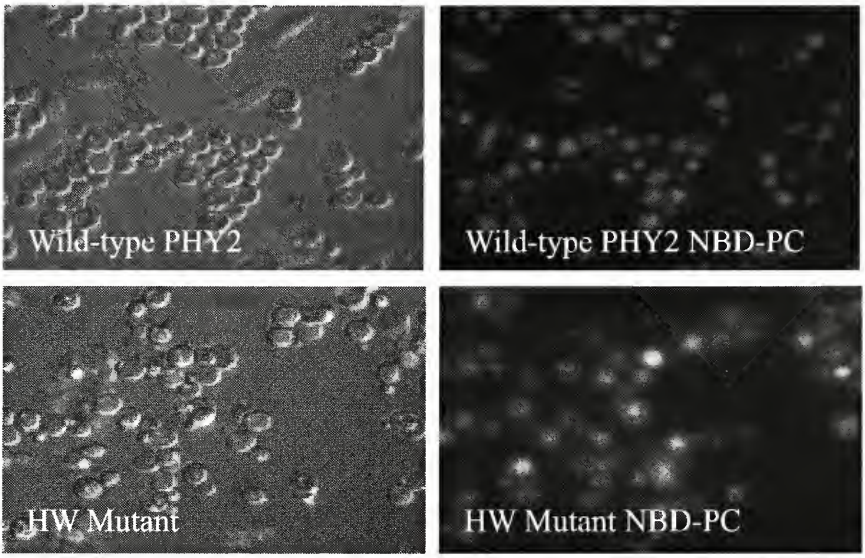



Figure 3: Lipid uptake of wild-type and HW mutants viewed by fluorescence microscopy. The pictures on the left show the strains under differential interference contrast, and the strains on the right show the strains under a fluorescence microscope. The strains had similar levels of fluorescence.

Discussion:

The HePC resistant strains were transformed with empty vectors and *LEM3* vectors and plated on SDC-ura+HePC in order to determine whether or not the strains had *LEM3* mutations. A lack of growth when the strains were transformed with *LEM3* meant that plasmid complementation occurred; the addition of a normal *LEM3* gene changed the phenotype back to normal, and the strain was no longer resistant to HePC. As shown in Figure 1, the known *LEM3*

mutant did not grow as well in the presence of HePC when it was transformed with a *LEM3* vector as it did when it was transformed with an empty vector (Fus). This pattern was also seen with HePC resistant mutant strains MB2, RS, and KM. These three mutants clearly exhibited better growth when transformed with an empty vector than when transformed with a *LEM3* vector. Therefore MB2, RS, and KM are *LEM3* mutants.

The HePC resistant mutant strains JG, HW, and HG had unclear plasmid complementation tests. An MIC assay was performed with these strains to better quantify any difference between their growth when transformed with an empty vector (Fus) versus when transformed with *LEM3* (*LEM3*). Graph 1 shows that the strains were affected by HePC at a similar concentration regardless of transformation with *LEM3* instead of an empty vector. Since the cells transformed with *LEM3* exhibited growth levels that were very similar to the growth level of the cells transformed with empty vectors, strains JG, HW, and HG are probably not *LEM3* mutants.

HePC resistant mutant strains JG, HW, HG, MB1, and TA were transformed with *PDRE* ß-gal. A transactivation assay was performed in order to determine whether or not their resistance to HePC was due to a PDR mutation. The production of ß-galactosidase was tied to the transcription of *PDR5*. Since *PDR1* and *PDR3* are transcription factors of *PDR5*, if they had hypermorphic mutations *PDR5* and lacZ (which is tied to the production of ß-galactosidase) would be transcribed more often. This would result in both more Pdr5p and more ß-galactosidase than the wild-type strain. A hypermorphic mutant would probably have ß-galactosidase activity between the levels of the wild-type and the *pdr3-11* (a very hypermorphic mutant) yeast. However, Graph 2 and Table 1 show that the presence of a PDR mutation in these mutants was difficult to determine because the mutants did not clearly exhibit the ß-galactosidase of the wild-type strain, but produced significantly less ß-galactosidase than the *pdr3-11* mutant. The P-values showed that all of the mutants were significantly different than the wild-type strain, except for MB1. Since MB1 had more ß-galactosidase activity than most of the other mutants, it appears that the number of

trials performed with each strain could have influenced the results.

Since the results of the transactivation assay were unclear, a few HePC resistant mutants were grown on cycloheximide plates as another test for PDR. MM never grew well enough when transformed with *PDRE* ß-gal to test with the transactivation assay; TA and HW were also tested. These strains were chosen because previous tests showed that their mutations were not completely dominant, meaning that they could be suitable for replica plating. As seen in Figure 2, MM grew well in the presence of cycloheximide, but TA and HW did not exhibit cycloheximide resistance. Since MM is resistant to HePC and cycloheximide, it probably has a PDR mutation. Previous experiments have also found that PDR mutations confer resistance to multiple drugs (Hallstrom 2001).

Fluorescence microscopy was performed on a wild-type strain and on the HePC resistant mutant HW. Wild-type and HW cells were placed in the presence of fluorescently labeled lipids; when the cells took in these lipids, they would also appear fluorescent. In Figure 3, pictures of the wild-type strain and HW were taken while they were being viewed with differential interference contrast (DIC) in order to show the approximate positioning of the cells. The pictures on the right half of the figure show the fluorescence given off by these cells. Other studies have shown that a mutation influencing uptake would be apparent by a difference in lipid uptake (Hanson 2003). The uptake of the fluorescently labeled lipids by the wild-type and HW cells appears to be equal. Therefore, HW probably does not have a mutation that alters its lipid uptake.

The HePC resistant mutant strain HW probably gained its resistance by a mutation other than a change in *PDR1*, *PDR3*, or *LEM3*. In order to further characterize the mutation of the HW strain, a dominance test should be performed. If the mutation is dominant, it would be very difficult to isolate. Then the mutant would be replica-plated with a genomic library. When the gene causing drug resistance is isolated, it could be run through a DNA sequencer. If it is found to be a novel mutation, further testing could be performed to study the mechanism by which the strain is resistant to HePC. The mutation that the strain has that resulted in HePC resistance could cause overproduction of the drug's intracellular target, alteration of

the target that disrupts binding and inhibition, degradation of the drug, inability of enzymes to change an inactive "pro-drug" to an active form, or compensation for the drug's effects.

TA, MB1, HG, and JG may also have mutations that were not due to a change in *PDR1*, *PDR3*, or *LEM3*. To determine if they have unique mutations, they would have to go through the same tests as HW.

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